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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO
09/339,922	06/24/99	HUSE	P-IX-3536

W
EXAMINER

023601
CAMPBELL & FLORES LLP
4370 LA JOLLA VILLAGE DRIVE
7TH FLOOR
SAN DIEGO CA 92122

HM22/0626

ART UNIT	PAPER NUMBER
1644	16

1644
DATE MAILED: 06/26/01

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 4/16/01

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1-33 is/are pending in the application.
Of the above, claim(s) 21-44 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 1-20, 25-33 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

–SEE OFFICE ACTION ON THE FOLLOWING PAGES–

* U.S. GPO: 1999-421-632/40206

SERIAL NO. 09/339,91
ART UNIT 1644

DETAILED ACTION

1. Applicant's election with traverse of Group I (claims 1-20 and 25-33) in Paper No. 15 is acknowledged. The traversal is on the ground(s) that it would not be an undue burden to search. This is not found persuasive because of the reasons of record set forth in Paper No. 11. Further, applicant's arguments are not found persuasive because of the inventions are independent (see MPEP 802.01, 806.04, 808.01) or distinct as claimed (see MPEP 806.05-806.05(I))) for the reasons of record set forth in the Restriction Requirement (Paper No. 12). The inventions require non-coextensive searches whether or not the classifications alone are coextensive.

The requirement is still deemed proper and is there FINAL.

Claims 21-24 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention.

3. Formal drawings have been submitted which comply with 37 CFR 1.84.

4. The application is required to be reviewed and all spelling and like errors corrected.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

5. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-3, 13-14 and 25-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

Given the Markush language of the claimed invention wherein the enhance LM609 grafted antibodies, and nucleic acids encoding said antibodies; there appears insufficient guidance and direction as to the predictability of enabling LM609 antibodies which can retain their binding to $\alpha v\beta 3$ or have enhanced binding to $\alpha v\beta 3$ by virtue of one particular change in a CDR.

The antigen binding properties of a given antibody are principally encoded within the primary and tertiary structure of hypervariable or complementarity determining regions (CDRs). As well as varying in sequence; the lengths and conformations of these loops differ from one antibody to the next. It is known that for each antibody; the antigen binding properties are etched into the tertiary architecture of the combining site, antibody structure itself guides the selection by via affinity in the screening assays, not based upon the primary amino acid sequence alone. There is high sterochemical complementarity between the surfaces of the bound antigen and the antibody combining site.

It has been well known to those skilled in the art at the time the invention was made that minor structural differences among structurally related compounds or compositions can result in substantially different pharmacological or biological activities.

For example, a single amino change in an immunoglobulin can have profound effects on the antigen bind specificity and properties of an antibody.

Without sufficient guidance, the changes which can be made in the structure of "enhanced LM609 grafted antibodies by relying on the change of one particular CDR and still provide enhanced ability to bind $\alpha v\beta 3$ is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue

7. Claims 1, 3, 4, 6, 7, 9, 10, 12, 13-20 and 25, 27, 29, 31, 26-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the "antigen binding fragments" such as those recited in claim 2, does not reasonably provide enablement for any "functional fragment" of the claimed enhanced LM609 grafted antibodies. The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims. Applicant has not provided sufficient direction or biochemical information on how to use "fragments" other than antigen-binding fragments. For example, a number of functional attributes have been attributed to the Fc component of an immunoglobulin. In addition, immunoglobulin fragments may be used to elicit specific antibodies responses, which, in turn, may be useful in generating specific antibody probes for various immunological procedures and assays. However there is insufficient direction and guidance in the specification on how to use such Fc fragments or other antigenic fragments of immunoglobulins. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe nor enable any "functional fragment" of the LM609 grafted antibodies other than antigen binding fragments.

8. Claims 1-3, 6, 9, 12-14, 25-26 and 33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is reminded that this is a written description rejection rather than an enablement rejection under 35 U.S.C. 112, first paragraph.

The instant claims are drawn to antibodies and nucleic acid molecules encoding said antibodies wherein the claims recited the following limitations:
"substantially the same" LM609 grafted antibodies;
LM609 grafted antibodies which comprise one particular "CDR" selected from a Markush
and/or nucleic acids encoding said antibodies; and
"Having the sequence".

Such antibodies and nucleic acid molecules encoding said antibodies do not meet the written description provision of 35 USC 112, first paragraph.

There is insufficient guidance and direction as to the written description of these antibodies which are substantially the same as another LM609 grafted antibody; these antibodies which rely upon a single "CDR" encompassed by the claimed products.

It is noted that "having the sequence" is considered open language, which would indicate that the sequences set forth in claim 33 comprise sequences both 3' and 5', including non-coding and coding sequences.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides (proteins) and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.
Thus, the specification fails to describe these DNA sequences. The Court further elaborated that generic statements are not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. Finally, the Court indicated that while applicants are not required to disclose every species encompassed within a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, defined by nucleotide sequence, falling within the scope of the genus, See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Therefore, there is insufficient written description for the "claimed limitations indicated above" other than a clear recitation of LM609 grafted antibodies and nucleic acids which encode said antibodies; which, in turn, rely upon a clear structure and $\alpha v\beta 3$ specificity under the written description provision of 35 USC 112, first paragraph.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001

9. Claims 1-20 and 25-33: It is apparent that the LM609 antibody is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the cell line / hybridoma which produces this antibody. See 37 CFR 1.801-1.809.

Given the disclosure (e.g. see column 15, paragraph 2) and the claims (e.g. see claims 3 and 16) encompassing the instant LM609 antibody produced by the hybridoma designated ATCC HB 9537 set forth in U.S. Patent No. 5,753,230 (1449); the conditions for the deposit of biological materials under 35 USC 112, first paragraph, with respect to LM609 have been satisfied.

10. Claims 3, 6, 9, 12, are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required tc cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

. It appears that the claimed recitation of "substantially the same" in the dependent claims broadens the claimed enhanced LM609 grafted antibodies.

11. Claims 1-20 and 25-33 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-20 and 25-33 are indefinite in the recitation of "LM609" because its characteristics are not known. The use of "LM609" grafted antibody antibodies as the sole means of identifying the claimed antibody / antibodies renders the claims indefinite because "LM609" is merely a laboratory designation which does not clearly define the claimed product(s), since different laboratories may use the same laboratory designations to define completely distinct cell lines .

Given that the LM609 is the referenced antibody in the claimed invention, applicant is invited to clarify the metes and bounds of LM609 in the context of the claimed invention.

B) Claims 1-20 are indefinite in the recitation of "enhanced LM609 grafted antibody" because the term "enhanced" is a relative term which renders the claims indefinite. The term "enhanced" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree and/or parameter(s) of "enhanced" is encompassed by the claimed invention, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention

C) Claims 3, 6, 9, 12 are indefinite in the recitation of "substantially the same" because the phrase "substantially the same" is a relative phrase which renders the claims indefinite. The phrase "substantially the same" is is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree and/or parameter(s) of "substantially the same" is encompassed by the claimed invention, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention

D) Applicant should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1-20 and 25-33 are rejected under 35 U.S.C. § 102(a) as being anticipated by Huse et al. (WO 98/33919; 144) (see entire document).

Huse et al. teach humanized LM609 antibodies and fragments thereof as well as nucleic acids encoding said antibodies and fragments, which encompass the limitations of the claimed invention (see entire document). Huse et al. teach that the selection of such LM609 antibodies is based upon their specificity and inhibitory properties for αvβ3; including modified and high affinity antibodies; which, in turn, are useful for diagnosis and therapy.

It appears that the instant SEQ ID NOS: 33, 34, 89, 90, 101, 102, 107, 108, 109, 110, 111 and 112 are disclosed in WO 98/33919.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced humanized LM609 antibodies, fragments thereof and nucleic acids encoding said antibodies.

15. Claim 1-20 and 25-33 are rejected under 35 U.S.C. § 102(b) as being anticipated by Wu et al. (PNAS 95: 6037-6042, 1998; 1449) (see entire document).

Wu et al. teach the stepwise in vitro affinity maturation of the αvβ3-specific humanized LM609 antibody; including the improved affinity of the antigen binding fragments of said LM609 variants as well as the construction of the CDR and combinatorial libraries and the screening of phage expression libraries for said LM609 variants.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced antibody variants and libraries comprising said antibody variants.

It is noted that the comparison of the instant products with prior art is difficult since the Office is not equipped to manufacture the claimed product and/or prior art products that appear to be same or nearly the same and conduct comparisons. The burden is on the applicant to establish a patentable distinction between the claimed and referenced LM609 variants and libraries comprising the nucleic acids encoding said LM609 variants. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

16. Claims 3, 6, 9, 12 are rejected under 35 U.S.C. § 102(e) as being anticipated by Brooks et al. (U.S. Patent No. 5,753,230; 1449) (see entire document).

Brooks et al. teach the LM609 antibody, including humanized LM609 antibodies (columns 15-18 and claims such as claim 12-13 and 30-31).

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced antibody variants and libraries comprising said antibody variants.

17. Claims 1-20 and 25-33 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Brooks et al. (U.S. Patent No. 5,753,230; 1449) OR Wu et al. (PNAS 95: 6037-6042, 1998; 1449) in view of art known gene cloning and expression strategies for deriving recombinant antibodies and fragments thereof, as disclosed on pages 8-39 or Examples I and II of the instant specification or as cited by references on the 1449.

Brooks et al. teach the LM609 antibody as well as humanized forms of this antibody and claim methods of using the LM609 antibody as well as humanized forms of this antibody (see entire document, particularly columns 15-19 and the claims).

Wu et al. teach the stepwise in vitro affinity maturation of the αvβ3-specific humanized LM609 antibody; including the improve affinity of the antigen binding fragments of said LM609 variants as well as the construction of the CDR and combinatorial libraries and the screening of phage expression libraries for said LM609 variants (see entire document, including Abstract, Materials and Methods, Results and Discussion).

The art known gene cloning and expression strategies for deriving recombinant antibodies and fragments thereof, are disclosed on pages 8-39 or Examples I and II of the instant specification or cited by references on the 1449 are of record.

With respect to enhanced LM609-specific antibodies and nucleic acids encoding said antibodies; given the teachings of humanized LM609 antibodies and art known methods to generate such humanized antibodies which retain the desired functional characteristics of the native antibody and to alter said antibody for therapeutic uses, including human therapy, as taught and known in the prior art.

Furthermore as pointed out above, Wu et al. teach that affinity maturation leads to the increased affinity of αvβ3-specific humanized LM609 antibody variants (see entire document).

As pointed out previously; the amino acid and nucleic acid sequences associated with the LM609 antibody including those of humanized LM609 antibodies and antibody variants with increased affinity for αvβ3 would have been available to the ordinary artisan, given the availability of the LM609 antibody and hybridoma together with general immunoglobulin gene cloning and expression strategies, including the affinity maturation schemes as taught by Wu et al.. It would have been have been a matter of routine experimentation well within the ordinary skill level of art to generate humanized LM609 antibodies and antibody variants thereof, DNA encoding said antibodies. Given the highly conserved nature of immunoglobulin gene organization and structure and the availability of probes and PCR primers for immunoglobulin gene cloning, one of ordinary skill in the art could have isolated the functionally rearranged heavy and light chain variable regions from the LM609 hybridoma cell line and determined their sequences with a complete expectation of success. For example, the ordinary artisan does not need to determine the amino acid sequences of a rearranged V (variable) region before cloning. The claims do not differ unexpectedly or unobviously from what one of ordinary skill in the art would have expected to obtain given the known LM609 hybridoma thereof, the known heavy and light chain and the art known techniques regarding the production of humanized antibody and antibody variants selected for higher affinity, as acknowledged by the number of available art known procedures disclosed in the instant specification and cited on the Information Disclosure Statement. .

In addition, Wu et al. Teach the construction and availability of the CDR and combinatorial libraries and the screening of phage expression libraries for LM609 variants (see entire document, including Materials and Methods).

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

18. The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 1-20 and 25-31 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the pending claims of copending application USSNs 08/791,391 and 08/790,540. It appears that the instant claims and the pending claims are drawn to the same or similar LM609 antibody and variants thereof, including those that read on instant SEQ ID NOS: 33, 34, 89, 90, 101, 102, 107, 108, 111, 112

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

20. Claims 1-20 and 25-31 are directed to an invention not patentably distinct from the pending claims of USSNs 08/791,391 and 08/790,540. Specifically, the conflicting claims are patentably distinct from each other because the pending claims are drawn similar or obvious variants of LM609-specific humanized antibodies, fragments and nucleic acids encoding said antibodies/fragments thereof

Commonly assigned USSNs 08/791,391 and 08/790,540., discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. § 103 if the commonly assigned case qualifies as prior art under 35 U.S.C. § 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 C.F.R. § 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application. A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. § 103 based upon the commonly assigned case as a reference under 35 U.S.C. § 102(f) or (g).

21. Claims 1-20 and 25-33 are provisionally rejected under 35 U.S.C. 103(a) as being obvious over copending USSNs 08/791,391 and 08/790,540 which have a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e) if patented. This provisional rejection under 35 U.S.C. 103(a) is based upon a presumption of future patenting of the conflicting application.

Specifically, the conflicting claims are patentably distinct from each other because the pending claims are drawn similar or obvious variants of LM609-specific humanized antibodies, fragments and nucleic acids encoding said antibodies/fragments thereof

This provisional rejection might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by a showing of a date of invention for the instant application prior to the effective U.S. filing date of the copending application under 37 CFR 1.131.

22. No claim is allowed.

It is noted that the particular recitation of LM609 antibodies comprising
the VH CDR1 referenced as SEQ ID NO: 34, the VH CDR2 referenced as SEQ ID NO: 102/104 and the VH CDR3 referenced as SEQ ID NO: 106
as well as the corresponding nucleic acids of
VH CDR1 referenced as SEQ ID NO: 33, the VH CDR2 referenced as SEQ ID NO: 101/105 and the VH CDR3 referenced as SEQ ID NO: 105 appear free of the prior art;
if applicant can distinguish the teachings of Wu et al. (PNAS 95: 6037-6042, 1998; 1449) from the instant claims

23. Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242 or (703) 305-7939.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1800 receptionist whose telephone number is (703) 308-0196.

PHILIP GAMBEL

Phillip Gambel, Ph.D.
Patent Examiner
Technology Center 1600
June 25, 2001